

WHAT IS CLAIMED IS:

1. A method for the preparation of  $F(ab')_2$  antibody fragments comprising the following steps:

- a) obtaining blood plasma from immunized mammals in septic conditions;
- b) contacting the plasma obtained with sterile pepsin in order to digest the antibodies;
- c) removing the albumin, fibrinogen and other undesirable substances present in the plasma or its digestion products;
- d) recovering the resulting  $F(ab')_2$  fragments from the solution; and
- e) optionally, purifying the  $F(ab')_2$  fragments thus obtained.

2. The method in claim 1 wherein step (c) comprises:

- a) adding between about 16% and about 22% (W/V) ammonium sulfate to the plasma to precipitate the albumin fibrinogen and their digestion fragments at a temperature of about  $55 \pm 4^\circ\text{C}$ ;
- b) cooling the solution to about 8 to about  $12^\circ\text{C}$  for at least two hours; and
- c) clarifying the solution and passing it through 12, 8 and  $4\mu$  tray filters.

3. The method in claim 1 wherein step (d) comprises:

- a) adding between about 32% and about 38% (W/V) ammonium sulfate to the solution at a pH of about  $6.8 \pm 0.2$  to recover all the  $F(ab')_2$  fragments from the solution;
- b) optionally, centrifuging the resulting suspension to eliminate the supernatant.

4. The method in claim 1, wherein step (e) comprises eliminating the salts and components of low molecular weight by means of dialysis or ultrafiltration of the  $F(ab')_2$ , making it possible to dissolve them.
5. The method in claim 1, wherein said steps of contacting, removing, recovering and purifying are conducted under aseptic conditions.
6. The method in claim 1, wherein the  $F(ab')_2$  binds a purified molecule.
7. The method in claim 6, wherein the purified molecule is a cytokine.
8. The method in claim 7 wherein the cytokine is selected from the group consisting of alpha tumor necrosis factor ( $TNF-\alpha$ ) and interferon- $\gamma$ .
9. The method in claim 8, wherein the cytokine is interferon- $\gamma$ .
10. The method in claim 8, wherein cytokine is alpha tumor necrosis factor ( $TNF-\alpha$ ).
11. The method in claim 1, wherein the  $F(ab')_2$  obtained binds and neutralizes a complex mixture of antigenic molecules.
12. The method in claim 11, wherein the mixture is the venom of a venomous animal.
13. The method in claim 12, wherein the venom is from a venomous animal selected from the group consisting of black widow spider (*Lactrodectus*

*mactans*), coral snake (*Micrurus nigrosinatus*), snake, scorpion and combinations thereof.

14. The method in claim 12, wherein the venom is from a coral snake (*Micrurus nigrosinatus*).

15. The method in claim 12, wherein the venom is from a black widow spider (*Lactrodectus mactans*).

16. The method in claim 12, wherein the venom is from scorpions selected from the group consisting of *Centruroides noxius*, *C. limpidus*, *C. limpidus tecomanus*, *C. suffusus suffusus* and combinations thereof.

17. The method in claim 12, wherein the venom is from snakes, the genera selected from the group consisting of Bothrops, Crotalus, Agkistrodon, Lachesis, Sistrurus and combinations thereof.

18. The method in claim 1, wherein the obtained  $F(ab')_2$  antibody fragments are free from albumin and complete antibodies, and substantially free of pyrogens.

19. A pharmaceutical composition comprising polyclonal  $F(ab')_2$  antibody fragments free from albumin and whole antibodies and substantially free of pyrogens, and an effective amount of a pharmaceutically acceptable carrier, wherein the  $F(ab')_2$  are obtained by means of the method of claim 1.

20. The pharmaceutical composition in claim 19 wherein the  $F(ab')_2$  binds a purified molecule.

21. The pharmaceutical composition in claim 20 wherein the purified molecule is a cytokine.

22. The pharmaceutical composition in claim 21 wherein the cytosine is selected from the group consisting of alpha tumor necrosis factor (TNF- $\alpha$ ) and interferon- $\gamma$ .

23. The pharmaceutical composition in claim 19 wherein F(ab')<sub>2</sub> neutralizes and binds a complex mixture of antigenic molecules.

24. The pharmaceutical composition in claim 23 wherein the mixture is the venom of a venomous animal.

25. The pharmaceutical composition in claim 24, wherein the venom is from a snake, the genera selected from the group consisting of black widow spider (*Lactrodectus mactans*), coral snake (*Micrurus nigrosinatus*), snake, scorpion and combinations thereof.

26. The pharmaceutical composition in claim 24, wherein the venom is from a snake, the genera selected from the group consisting of Bothrops, Crotalus, Agkistrodon, Lachesis, Sistrurus and combinations thereof.

27. The pharmaceutical composition in claim 24, wherein the venom is from scorpions selected from the group consisting of *Centruroides noxius*, *C. limpidus*, *C. limpidus tecomanus*, *C. suffusus suffusus* and combinations thereof.

28. The pharmaceutical composition in claim 24, wherein the venom is from a coral snake (*Micrurus nigrosinatus*).

29. The pharmaceutical composition in claim 24, wherein the venom is from a black widow spider (*Lactrodectus mactans*).

30. A pharmaceutical composition comprising polyclonal F(ab')<sub>2</sub> antibody fragments free from albumin and whole antibodies and substantially free of pyrogens, wherein the F(ab')<sub>2</sub> binds to a purified molecule.

31. The pharmaceutical composition of claim 30, wherein the purified molecule is a cytokine.

32. The pharmaceutical composition of claim 31, wherein said cytokine is TNF- $\alpha$ .

33. The pharmaceutical composition of claim 32, wherein said F(ab')<sub>2</sub> neutralizes said TNF- $\alpha$ .

34. A pharmaceutical composition comprising polyclonal anti-TNF- $\alpha$  F(ab')<sub>2</sub> antibody fragments free from albumin and whole antibodies and substantially free of pyrogens.

35. A composition comprising the composition of any of claims 30 to 34, further comprising a pharmaceutically acceptable carrier.

36. A pharmaceutical composition comprising polyclonal F(ab')<sub>2</sub> antibody fragments free from albumin and whole antibodies and substantially free of pyrogens, wherein the F(ab')<sub>2</sub> antibody fragments are obtained by the method which comprises:

a) contacting a source of antibody with pepsin under conditions to prepare an antibody digest containing F(ab')<sub>2</sub> fragments and being substantially free of unhydrolyzed antibodies;

b) treating said antibody digest by two steps of ammonium sulfate precipitation, i) one step at about 16% to about 22% weight by volume ammonium sulfate; and ii) another step at about 32% to about 38% weight by volume of ammonium sulfate.

37. A method of treating a cytokine-mediated immune reaction a patient in need thereof, which comprises parenterally administering to said patient a therapeutically effective amount of the pharmaceutical composition any of claims 30 to 34.

38. The method of claim 37 wherein said parenteral administration comprises systemic administration.

39. The method of claim 38, wherein said systemic administration comprises intravenous administration.

40. The method of claim 38, wherein said systemic administration comprises intramuscular administration.

41. The method of claim 37, wherein said parenteral administration comprises intraperitoneal administration.

42. The method of claim 37, wherein said patient is a human who has been exposed to the venom of a poisonous animal.

43. The method of claim 37, wherein said parenteral administration is repeated at least once.